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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,482	02/29/2000	YEN CHOO	PM264974	8038
20350	7590	01/27/2005	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			WESSENDORF, TERESA D	
			ART UNIT	PAPER NUMBER
			1639	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/424,482

Applicant(s)

CHOO ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6,7,27 and 28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 6-7 and 27-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Information Disclosure Statement

Applicants state that applicants are unable to find any notification from the examiner that the references were not received, nor any request from the examiner for re-submission of the references.

In response, attached to the restarted Office of 12/02/03 was an Interview Summary Record. In the Interview Summary Record the examiner left two messages requesting for the references prior to the issuance of a First Office action. [The Interview Summary record is again attached herein.]

Priority

Applicants are not entitled to the priority date of the United Kingdom(9710809.6) ('809.6 application) filed on May 23, 1997 because the specification does not disclose the subject matter of claim 1. The claim that is not supported in the foreign priority '809.6 application, specifically the ".....randomization extends to cover at least one position selected from the group consisting of -1, 1, 2, 3, 5, and 6 and at least one position selected from the group consisting of -1, 1, 2 and 3 in first and second adjacent fingers, respectively and wherein the randomization is at least at positions 6 and 2 of the adjacent first and second fingers, respectively." In the

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amendment of 3/25/03, the as-filed specification was amended to the present claim 1. The claim "and wherein the randomization is at least at positions 6 and 2 of the adjacent first and second fingers, respectively" is not in claim 1 but a limitation of the then newly added claim 26 (and claims 27-28). In the REMARKS of 3/25/03 amendment, applicants point out support in the instant specification. Since it was supported in the U.S. national application, claiming priority to the PCT, then the specification of the foreign '809.6 application was assumed to be the same. However, upon review of the '809.6 application, said limitation was not supported. The inadvertent omission of reviewing the priority '809.6 document is regretted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1, 2, 6-7 and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greisman et al (Science, Ref 97) in view of and Choo et al (Current Opinion in Biotechnology).

Greisman et al discloses at page 275, the abstract a library of zinc finger that extends to the 9 to 10 base pair target site, adding and optimizing one finger at a time. The amino acid residues are randomized at positions -1, 1, 2, 3, 5 and 6 in each of the alpha helices (Fig. 1) of the three finger of the zinc finger, ZIF268. See further Fig. 2B where a random residues at Finger 1 is at position -1, 2, 6 and Finger 2 at -1, 2, 3 and at Finger 3 at -1, 2 and 6. The optimized library is produced by the extension or incorporation of the selected randomized finger into the next set. Greisman does not disclose randomization such that the randomization extends to at least one position selected from the group consisting of -1, 1, 2, 3, 5 and at least one position selected from the group consisting of -1, 1, 2 and 3 in the first and second fingers, respectively and wherein randomization is at least at positions 6 and 2 of the adjacent first and second fingers, respectively. Choo discloses at page 432, col. 2 a library of a middle finger in which the seven positions(-1, 1, 2, 3, 5, 6 and 8)were randomized. Choo further discloses at page 433 last paragraph that the best

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combination of fingers was selected en bloc using the entire 9bp target site. The strategy of a further round of selection en bloc following the combinatorial assembly of fingers selected in a previous round singles out the DNA-binding domain containing the most favorable combinations of available finger, thus, partly circumventing the problems of position and context. It would have been obvious to one having ordinary skill in the art at the time the invention was made to extend the randomization of residues in the library of Greisman en bloc as taught by Choo. Greisman already suggests that at least at one position of -1, 1, 2, 3, 5 of the first finger and at least one position -1, 1, 2, and 3 at the second adjacent finger can be random residue. The advantage provided by Choo provides the motivation to do the modification to one having ordinary skill in the art.

Response to Arguments

Applicants do not agree with the Examiner's position, as to the lack of support in the United Kingdom foreign priority '809.6 application. But states that the issue is moot because the Isalan et al. reference is not prior art.

In response, in view of applicants' arguments, the Isalan no longer apply. However, even without, Isalan the claimed

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invention is prima facie obvious over the teachings of Greisman in view of Choo et al.

Applicants state that the Greisman and Choo references were extensively discussed in Applicants' Appeal Brief (dated September 16, 2003). Insofar as the Examiner's comments regarding these references are inconsistent with Applicants' comments in the Appeal Brief applicants respectfully disagree.

At page 10 of the Appeal Brief, applicants argue that Greisman involves randomizing and selecting one finger at a time (see col. 5, lines 37-40). Greisman's method is performed in an iterative fashion in which fingers) that have previously been selected provide context for selection of another finger (see claim 1). In brief in a first step, a zinc finger protein comprising one randomized finger and two constant fingers is selected. In a second step, a second zinc finger protein comprising one randomized finger, one previously selected finger, and one constant finger is selected. In a third step, a zinc finger protein comprising one randomized finger and two previously selected fingers is selected. The iterative method of selection, although more elaborate, has the advantage that new fingers are selected in a relevant structural context (col. 6, lines 66-67). It is argued that Griesman differs from the present claims in not describing a library of zinc finger

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proteins in which at least two fingers (much less two adjacent fingers) of the proteins have been simultaneously randomized. The cited references take a different approach in providing libraries in which only one finger of a zinc finger protein is randomized. After separate selection of each finger, the fingers are joined in a modular fashion to form a zinc finger protein that binds to a desired target sequence.

In reply, applicants' arguments with respect to the method of Greisman are not commensurate in scope with the claims. The claims do not recite for a method by which the zinc finger proteins are obtained. Greisman at page 658, Fig. 1 A shows a random Finger at -1 to 6 positions. Greisman states "randomized positions (circled) correspond to residues -1, 1, 2, 3, 5, and 6 in each of the α helices and include every position that makes a base contact in one of the known zinc finger-DNA complexes...". Figure B, *ibid*, shows a random finger protein with Finger 1 having random residues at positions -1 and 6 and Finger 2 at positions -1, 2 and 3. Greisman therefore discloses or at least suggests, the claimed zinc finger polypeptide library with random positions at -1 to 6 in the first finger and -1, 1, 2 and 3 in the second finger. At least position 6 and position 2 of the adjacent first and second fingers are at least random. As applicants' acknowledge above, Greisman's iterative process,

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obviously extends the randomization at the different positions -1 to 6 of the first finger and -1 to 3 of the second finger, albeit one at a time. Choo as stated provides the motivation to extends the randomization en bloc.

Applicants at page 13 of the Brief acknowledge that Choo at page 433 discloses "the most obvious strategy is to simultaneously randomize each finger in a multifinger library ..such that screening with target DNA results in selection of an entire DNA-binding domain. Importantly, because multiple fingers are selected en bloc, each will be optimized according to its position and context within the DNA-binding domain..." But argue that the reference rejects this strategy as being "unlikely to be practical in the near future."

In reply, the statement that is unlikely to be practical in the near future does not apply to the theoretical size of a full library of three fingers, each comprehensibly randomized in four positions. However at the last paragraph of page 433 Choo positively employ and discloses that the best combination of fingers was selected en bloc using the entire 9bp target site. The strategy of a further round of selecting en bloc following the combinatorial assembly of fingers selected in a previous round singles out the DNA-binding domain which contain the most favorable combinations of available fingers, thus partly

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circumventing the problems of position and context. Furthermore, at page 435, col. 1 Choo positively recites a combinatorial assembly of individually selected fingers, followed by selection of DNA binding domain en bloc. Since Greisman discloses the residues that can be randomized hence, it would be expected that en bloc random residues would produce the advantageous results as taught by Choo. The combined teachings of Greisman and Choo therefore render the claimed invention prima facie obvious. As held by the majority in *Merck & Co. Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 10 USPQ 2d 1843 (Fed. Cir. 1989), at 10 USPQ 2d 1846: That the '813 patent discloses a multitude of effective combinations does not render any particular formulation less obvious. This is especially true because the claimed composition is used for the identical purpose taught by the prior art. See *In re Corkill*, 771 F.2d 1496, 1500, 226 USPQ 1005, 1008 (Fed. Cir. 1985).

No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be

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reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw

January 24, 2005